REMARKS

Claims 2-9, 11, and 22-25 are pending in the instant application. In view of the following remarks, reconsideration of the application is respectfully requested.

The Examiner has maintained the rejection of claims 2-5, 7-9, 11, 22, 23, and 25 as allegedly unpatentable over Ferrara *et al.* (US 6,455,283) under 35 U.S.C. § 103. The Examiner has also maintained the rejection of claims 6 and 24 as allegedly unpatentable over Ferrara in view of Bentz *et al.* (EP 0 512 844 A1). The Examiner cites to "reasons of record set forth in the previous Office Actions mailed 8/22/07 and 1/25/08," and further cites to Uutela *et al.* (US 7,105,481).

In particular, the Examiner cites to Uutela *et al.* (US 7,105,481) as allegedly supporting the assertion that "determining the structural-functional relationship of a newly discovered protein was routine." The Examiner asserts that Uutela "provides not only 'obvious to try,' but also motivation to make the truncated form of the molecule as claimed, and expectation of success." (*See* Advisory Action at p. 2.) The Examiner states that Uutela discloses PDGF-D, which is closely related to PDGF-C in the instant application, and also states that Uutela teaches that PDGF-C and PDGF-D have a two domain structure comprising an N-terminal CUB domain and a C-terminal PDGF/VEGF homology domain; that PDGF-C "requires proteolytic removal of the N-terminal CUB domain for receptor binding"; and that "the truncated homodimer PDGF-DD retains ... functional activity." The Examiner further contends that this example "clearly demonstrates that determining the structural-functional relationship of a polypeptide, and making functional fragments thereof are both desirable and routine in the art." (*See id.*)

Applicants initially note that the Uutela disclosure cited by the Examiner – relating to a two-domain structure for PDGF-C and PDGF-D – is not prior art to the instant application. Uutela claims the benefit of eight prior applications, only one of which – U.S. provisional application 60/107,852 (attached hereto) – was filed prior to Applicants' effective filing date of December 7, 1998. The '852 provisional application does not disclose a two domain structure for either PDGF-C or PDGF-D. Indeed, the '852 application discloses only a small fragment of PDGF-C (corresponding to residues 283-345 of Applicants' SEQ ID NO:2; *see* '852 application at Figure 3) and, similarly, only a small fragment of PDGF-D (corresponding to residues 305-370 of SEQ ID NO:8

of the cited Uutela patent; *see* '852 application at Figures 2 & 3.) Neither of these fragments include the full growth factor domain for the respective PDGF-C and PDGF-D proteins. Accordingly, the '852 application does not teach or suggest a "truncated form of PDGF-D comprising residues 254-370 of SEQ ID NO:8," nor does the '852 application teach or suggest a corresponding truncated form of PDGF-C.

For these reasons, because Uutela's discussion of a two-domain structure for PDGF-C and -D is not prior art to the instant application, Uutela cannot serve as a basis for establishing that Applicants' instantly claimed invention was "obvious to try" to one of ordinary skill in the art as of Applicants' effective filing date, nor can it serve as a basis for establishing a motivation to make a truncated form of PDGF-C as claimed. Furthermore, Uutela cannot serve as basis for showing a reasonable expectation of success as of Applicants' effective filing date.

Nor does Uutela otherwise support the contention that determining the structural-functional relationship of a PDGF-C or PDGF-D polypeptide, and making functional fragments thereof, were "routine in the art." In this regard, the Uutela reference is not representative of the ordinary skill in the art with respect to the characterization of PDGF-C and PDGF-D. Applicants note that the inventive entity of the Uutela patent, including the claimed priority applications, includes Dr. Ulf Eriksson, a Member of the Ludwig Institute for Cancer Research ("LICR"). (*See* Exhibit 1, "LICR Stockholm Branch Research Group – Tissue Biology Group, Ulf Eriksson," *http://www.licr.ki.se/D_groups/d2_Tissue-Biology.php*, downloaded June 19, 2008.) Dr. Eriksson's research has been particularly focused on the PDGF/VEGF family of growth factors, including PDGD-C and PDGF-D. (*See* Exhibit 1.) Indeed, Dr. Eriksson is also a named inventor of U.S. Patent Application Publication No. US2002/0164687, which relates to PDGF-C and was previously cited in the Office Action dated 1/12/2007. As evidenced by the long chain of claimed priority applications for the Uutela patent and US2002/0164687, Dr. Eriksson has been involved in research relating to PDGF-C and -D since around the time of the inception of this scientific field. In addition, Dr. Eriksson has an extensive body of published work relating to the PDGF/VEGF growth factor family that predates the identification of PDGF-C and PDGF-D, dating back to at least 1996. (*See* Exhibit 2, PubMed Search Results for VEGF and Eriksson U,

http://www.ncbi.nlm.nih.gov/sites/entrez, downloaded June 24, 2008; Exhibit 3, PubMed Search Results for PDGF and Eriksson U, *http://www.ncbi.nlm.nih.gov/sites/entrez*, downloaded June 24, 2008.) Furthermore, as evidenced by Dr. Eriksson's co-authorship of research publications in the area of PDGF-C and PDGF-D since the identification of these molecules, Dr. Eriksson has continued to advance the knowledge in the art relating to PDGF-C and PDGF-D. (*See* Exhibit 4, PubMed Search Results for PDGF-C and Eriksson U, *http://www.ncbi.nlm.nih.gov/sites/entrez*, downloaded June 24, 2008; Exhibit 5, PubMed Search Results for PDGF-D and Eriksson U, *http://www.ncbi.nlm.nih.gov/sites/entrez*, downloaded June 24, 2008.)

Accordingly, Dr. Eriksson is a person of particularly high expertise with regard to PDGF/VEGF growth factor family members, including PDGF-C and -D. In light of Dr. Eriksson's high level of expertise in this area, the inventive entity of the cited Uutela reference cannot be considered as representative of an ordinarily skilled artisan, and thus the scientific work discussed in Uutela relating to PDGF-C and -D cannot be presumed *a priori* to have been "routine" in the art. For at least this reason, in addition to reasons previously discussed, the cited Uutela patent does not support the Examiner's contention that "determining the structural-functional relationship of a newly discovered protein was routine."

In addition, and irrespective of the level of skill associated with the Uutela disclosure, the disclosures of the Uutela priority applications further demonstrate that determining the structural-functional relationship of the PDGF-C or PDGF-D growth factor domain was not routine. Applicants respectfully refer the Examiner to Uutela's U.S. Provisional Application 60/113,997, filed December 28, 1998 (the "'997 application"; attached hereto). Although the '997 application discloses polypeptides that can be aligned with Applicants' SEQ ID NO:2 (*see* Figure 5 – "hVEGF-F") or Uutela's SEQ ID NO:8 (*see* Figure 4; *see also* Figure 5 – "hVEGF-G"), this document does <u>not</u> disclose a fragment of either polypeptide corresponding to the growth factor domain of PDGF-C or PDGF-D (*see* '997 application, *passim*).

Indeed, it is not until Uutela's later filed U.S Provisional Application 60/150,604 (the "'604 application") that Uutela *et al.* discuss even the possibility of an active C-terminal fragment of PDGF-D. (*See* '604 application [attached hereto] at p. 23,

first full paragraph.) Applicants further note that the '604 application was filed August 26, 1999, almost 8 months after the filing of the '997 application. Applicants submit that this eight month period – from Uutela's first disclosure of a polypeptide that includes residues 254-370 of Uutela's SEQ ID NO:8 until Uutela's first discussion of the possibility of an active C-terminal fragment – further demonstrates that determining the structural-functional relationships for PDGF-D or PDGF-C was not a routine matter.

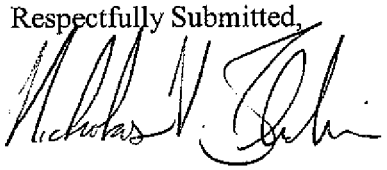
Applicants further note that Uutela does not address Applicants' previous arguments regarding unexpected results showing non-obviousness of the claimed invention.

For the reasons above, in addition to reasons already of record as set forth in the Amendments dated 3/25/2008 and 11/9/2007, claims 2-5, 7-9, 11, 22, 23, and 25 are patentable over Ferrara *et al.* under 35 U.S.C. § 103. For essentially the same reasons, because Bentz *et al.* does not cure the deficiencies of Ferrara as set forth in Applicants' previously-filed Amendments, claims 6 and 24 are patentable over Ferrara in view of Bentz. Accordingly, withdrawal of the present rejections is respectfully requested.

CONCLUSION

On the basis of the above remarks, Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6558.

Respectfully Submitted,



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Attachments: Exhibits 1-5
Copy of U.S. Provisional Application No. 60/107,852
Copy of U.S. Provisional Application No. 60/113,997
Copy of U.S. Provisional Application No. 60/150,604
Request for Continued Examination (RCE) under 37 C.F.R. § 1.114
Petition for Extension of Time under 37 C.F.R. § 1.136(a)

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